(b) determining whether to provide notice of a clinical study related to said disease condition;

C5 cont'd

(c) providing a web interface for submitting answers to a screening questionnaire associated with said clinical study; and,

(e) storing said answers in the database.

REMARKS

Claims 1-15 and 121-128 are pending. Claims 1 and 121-128 are hereby cancelled without prejudice to or disclaimer of the subject matter claimed therein. Applicants reserve the right to file a continuation or divisional application directed to the cancelled claims. Claims 2-5, 7-13 and 15 have been amended. Support for these amendments can be found throughout the specification and claims as originally filed. Claims 129-151 have been added. Support for the new claims can be found throughout the specification and claims as originally filed, particularly from page 20 line 21 to page 22 line 7. No new matter has been introduced. With this amendment, claims 2-15 and 129-151 are pending.

The specification has been amended to correct an obvious typographical error. No new matter has been introduced.

In the event that extensions of time beyond those petitioned for herewith are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned. Applicants do not believe any additional fees are due in conjunction with this filing. However, if any fees under 37 C.F.R. 1.16 or 1.17 are required in the present application, including any fees for extensions of time, then the Commissioner is hereby authorized to charge such fees to Arnold & Porter Deposit Account No. 50-2387, referencing matter number 16602.003.

Claim rejections – 35 U.S.C. 112, second paragraph.

Claim 4 stands rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention because the claim recites the limitation "the questionnaire" without sufficient antecedent basis for that phrase. Applicants have now amended claim 4 to depend from claim 2 instead of claim 1. Claim 2 contains the necessary antecedent basis for this element in claim 4. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

Claim rejections – 35 U.S.C. 103

Claims 1 and 121-128 have been cancelled without prejudice to or disclaimer of the underlying subject matter disclosed therein. Therefore, withdrawal of the rejections of these claims is respectfully requested.

Claims 2-5 and 7-12 stand rejected under 35 U.S.C. 103(a) as allegedly unpatentable over information published at www.centerwatch.com (hereinafter CenterWatch) in view of Colon *et al.*, U.S. Pat No. 5,991,731 (hereinafter Colon). Applicants respectfully disagree.

The Combination of Colon and CenterWatch Is Improper

Initially, Applicants disagree with the Examiner's use of the CenterWatch material as prior art. The CenterWatch reference cited by the Examiner purports to be printouts of cached web pages. The dates of the printouts are November and December of 2002. While the printouts include various copyright dates earlier than 2002, it is impossible to know whether the content of the web site contained in those printouts has been altered since the copyright date. Applicants note that, unlike a book or other publication, the content of a website is easily amended and is typically amended with no indication on the face of the website what changes have been made. Further, the printout has no publication number or any other publicly accessible reference number. The public, and therefore the Examiner, cannot be sure how much of the subject matter contained in the printouts was publicly available before November of 2002. The status of this

document as prior art, at least in the form printed in November or December of 2002, has therefore not been demonstrated. Applicants accordingly submit that it is improper for the Examiner to apply it against the pending claims and respectfully request that the Examiner withdraw all rejections relying on the CenterWatch printouts.

Further, in forming each of the rejections the Examiner has combined CenterWatch with Colon, relying on Column 1 lines 42-51 of Colon for an alleged motivation to combine of "automatically assigning thousands of participants in a clinical study with respect to care strategies to be administered to study participants". E.g., Office Action at page 5. However, the cited portion of Colon on which the Examiner relies is a statement from Colon's summary of his own invention. Thus, that statement in Colon suggests only that the art should look to the disclosure of *Colon*. Surely, Colon's description of his own invention cannot be read to imply that those of ordinary skill in the art should look elsewhere for what Colon alleges is his advance over the art.

Moreover, even assuming that those of ordinary skill in the art would have been motivated from Colon's summary of his own invention to "automatically assign [] thousands of participants in a clinical study with respect to care strategies to be administered to study participants", that hardly indicates a motivation to do so using the particular system described in CenterWatch. It is well established that for two art references to be combined and used to render an invention obvious, there must be some motivation to combine them. *In re: Jones*, 958 F.2d 347 (Fed. Cir. 1992).

Finally, Applicants submit that the combination of Colon and CenterWatch is improper for yet the further reason that the database of Colon would be inoperable with the Center Watch system without some modification being made to it. Colon's database randomly enrolls, or randomizes, a number of participants who have already been clinically evaluated for a particular clinical study in the various arms of the study without revealing the randomization to either the patient or the administering physician. Indeed, such information cannot be revealed to the patient or physician without compromising the clinical data that is the purpose of the study. CenterWatch, on the other hand, is intended to inform potential participants of available clinical

studies, and enable them to begin a dialogue with the enrolling physician, similar to a computerized classified advertisement. Thus, in order to use the database techniques of Colon in the system of CenterWatch one would need to modify those database techniques so that the users would not receive randomized clinical study information. The Examiner, of course, has no writing before him – other than Applicants' disclosure – that even arguably suggests such a modification. Certainly, the mere fact that the prior art could be modified would not have made the modification obvious unless the prior art suggested the desirability of the modification itself. *In re: Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984).

Even if the database in Colon were altered to be useful in the present invention, it would no longer be operable for its originally intended purpose. Altering Colon to give the results to the potential clinical study participants would invalidate its intended purpose of *not* revealing its results to the patient. As the Federal Circuit has noted, it is impermissible to use elements of a reference in formulating a rejection in a manner that would render them inoperable in their native environment. *In re: Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984). Indeed, such a reference is considered to teach away from such modifications. *Id.* In short, those of ordinary skill in the art simply would not combine the database of Colon with the system of CenterWatch. That combination therefore cannot render the claims unpatentable. Accordingly, Applicants assert that the combination of Colon and CenterWatch is improper.

The Combination of Colon and CenterWatch Does Not Render The Claims Unpatentable

Even were it proper to combine CenterWatch and Colon, Applicants submit that the combination does not render the pending claims unpatentable. For example, amended claim 2 expressly recites the step of:

> (e) automatically presenting a questionnaire associated with the given clinical study to the person or caregiver after step (d);

Note that the claimed questionnaire is "automatically" presented, is presented after notice is given of a particular clinical study (see step (d)), and is associated with that study.

Neither Colon nor CenterWatch teach or suggest a method with such a step. In Colon, for example, no notice is given of a particular clinical study, as Colon is not directed to providing a prospective study participant with access to a plurality of different potential studies. Rather, Colon discloses a system for determining whether a person is eligible for a single study. No "notice" functionality is therefore disclosed because no such functionality is meaningful in that system. Further, while in Colon follow up information can be entered into a database on a follow-up visit, see col. 7, l. 8 et seq., there is no indication that the data fields into which such information is entered are presented "automatically". Quite the contrary, Colon expressly states that the follow-up visit requires "starting up and initializing the system". Col. 7, l. 11, Figure 6, block 71.

Similarly, CenterWatch provides no questionnaire whatsoever after notice is given the user and certainly not one about a particular clinical study.

Each of the other pending claims contains similar language, though somewhat different in scope. For example, claims 138, 139, 150 each contain the step of "presenting a screening questionnaire associated with said clinical study", in which "said clinical study" is the study for which notice has been given. Neither Colon nor CenterWatch provide a screening questionnaire associated with a particular study after notice of that study is given. Colon gives no notice whatsoever and CenterWatch permits the entry of non-notice specific data only *before* notice of a study is provided.

Similarly, claim 140 reads as follows:

> 140. (New) A method of administering a database comprising the steps of:
> (a) storing in a computer memory information indicating whether notice of one or more clinical studies associated with a particular disease condition is desired and registration information that indicates at least a geographic location, said disease condition of interest, and contact information; and,
> (b) storing in said memory responses to a questionnaire associated with said notice.

Claim 149 reads as follows:

149. (New) A computer readable medium comprising a database created by performing the steps of:

(a) storing in a computer memory information indicating whether notice of one or more clinical studies is desired and registration information that includes at least a geographic location, a disease condition of interest, and contact information; and,

(b) storing in said memory responses to a screening questionnaire associated with said notice.

Thus, each of these claims requires the storage of responses to some type of questionnaire associated with a notice of a particular clinical study. They therefore also distinguish the cited art.

Similarly, claim 151 includes the step of "providing a web interface for submitting answers to a screening questionnaire associated with said clinical study", which study had been the subject of a determination of whether to provide notice to the user.

Claim 129, while slightly different, is also distinguishable. That claim includes the step of "allowing the person or caregiver the opportunity to amend the registration information in the database during a subsequent visit to the web site." Neither Colon nor CenterWatch disclose such functionality

Accordingly, each of these claims and their dependents are distinguishable from the cited combination for at least the reasons cited immediately above.

Moreover, the various dependent claims recite additional elements that distinguish them from the Examiner's combination. For example, claim 3 includes the following language:

> (g) Accessing the information stored along with other information in the database to determine whether the person qualifies to participate as a subject in a clinical study different from the given clinical study after step (f).

Neither CenterWatch nor Colon teaches the use of responses to a questionnaire along with other information in the database to determine whether the person qualifies to participate as a subject in a clinical study. To the contrary, Colon requires the physician to enter data previously provided during an initial patient interview. Nothing in either Colon or CenterWatch teaches or

suggests this type of screening functionality expressly included in claim 3.

Similarly, claim 4 includes a further refinement of the questionnaire:

> wherein the questionnaire includes criteria specific to a clinical study for determining whether the person is an eligible subject for the given clinical study.

Colon does not disclose this element.

The input block of Colon, to which that citation refers, takes only follow-up data, end-point data and significant events data and is used only to determine whether or not the prescription dosage for a current study participant should be adjusted. Colon, column 7 lines 8-37. It says nothing of "criteria specified by a sponsor of the clinical study for determining whether the person is an eligible subject for the given clinical study". Indeed, the person in Colon for whom the data is entered is already a subject in a clinical study.

For a similar reason the cited art does not teach or suggest the following element of claim 5:

> step (d) includes notifying the person or caregiver of the given clinical study during a current or subsequent visit of the person or caregiver to the web site.

The Examiner cites Colon column 6 lines 39-50 for such a teaching. However, the database in Colon is not used to screen for potential clinical trial participants. Nor does the disclosure of Colon column 6 lines 39-50, inform the person or caregiver themselves of anything. The user of the database in Colon is the physician, not the person or caregiver, so even if Colon did teach notifying the user of clinical studies, it would still not teach notifying the person or caregiver. In addition, Colon does not suggest modifying the database in such a way as to perform the steps of claim 5.

Regarding claims 8 and 9, the Examiner concedes that CenterWatch and Colon do not disclose:

> wherein the notice provided in step (d) is sent by regular mail to the person or caregiver

or

wherein the notice provided in step (d) is communicated by telephone to the person or caregiver.

However, the Examiner takes "official notice" that it was well known in the electronic arts to send requested notice information to a requestor via mail or by telephone and states that the motivation for delivering notice by such media is for the convenience of the requestor.

Applicants respectfully disagree that an application of regular mail or telephone in claims 8 or 9 is obvious. The Examiner has not indicated why it would have been obvious to use regular mail or telephone for a transaction that is otherwise completely electronic. The Examiner simply stated that the purpose of using such media would be for the convenience of the user. Applicants assert the opposite. Convenience has dictated that correspondence ***not*** take place using regular mail or the telephone, but instead take place electronically. The trend in communication, especially communication using the Internet, is to have the entire transaction occur electronically, without any use of regular mail or telephone. Withdrawal of these rejections is respectfully requested.

Regarding claim 11, the Examiner alleges that CenterWatch discloses: wherein in step (c) a determination is made not to provide the person or caregiver with the notice of the given clinical study. Applicants respectfully disagree. The Examiner has not indicated where in CenterWatch a determination is made not to provide the person with notice. Lacking such an indication by the Examiner, claim 11 is not rendered obvious by CenterWatch. Withdrawal of the rejection is respectfully requested.

Regarding claim 12, the Examiner alleges that CenterWatch discloses: wherein in step (a) the registration information includes a user id, a password, electronic mail address or telephone number, zip code, first name or preferred name, gender, date of birth, whether the person is interested in clinical study information, new medical therapies, or participating in clinical studies. Applicants respectfully disagree. However, to facilitate prosecution, claim 12 has been amended and whatever else CenterWatch discloses, CenterWatch does not disclose the elements of amended claim 12. Withdrawal of the rejection is respectfully requested.

Claims 6, 13, and 14 stand rejected over Colon and CenterWatch in addition to Clinmark and claim 15 stands rejected over Colon and CenterWatch in addition to Larkin.

Neither Clinmark nor Larkin, in combination with Colon and CenterWatch, make obvious any of the independent claims from which claims 6, 13, 14 or 15 depend. As discussed above, the combination of Colon and CenterWatch does not suggest any of the claims from which claim 6, 13, 14, and 15 depend. Clinmark and Larkin cannot supply what CenterWatch and Colon lack. Consequently, claims 6, 13, 14 or 15 are not obvious.

Specifically, claim 6 stands rejected over CenterWatch and Colon as applied to claim 5 and further in view of Clinmark. The Examiner alleges that Clinmark discloses:

> wherein step (d) further includes providing a listing of information associated with the given clinical study in a personal library associated with the person or caregiver on the web site.

The article, however, does not mention anything about providing a listing of information associated with the given clinical study in a personal library associated with the person or caregiver. In fact, most of the article discusses how *investigators and sponsors* are the primary users of the web site. The only mention of individuals in the article occurs in the third to last paragraph (which the Examiner cites as containing a reference to bulletin boards). An electronic bulletin board or anything described in the paragraph referring to individuals does not have anything to do with providing a listing of information associated with a given clinical study in a personal library associated with the person or caregiver.

Further, the Examiner states that the motivation to combine these references is to provide a forum for individuals with a common purpose to learn about trends and exchange information. Again, whether that is so or not, it certainly has nothing to do with providing a listing of information associated with the given clinical study in a personal library associated with the person or caregiver on the web site. The Examiner has not indicated any motivation to combine its bulletin board or any other forum for individuals with a common purpose to learn about trends and exchange information with the teachings of CenterWatch. CenterWatch certainly says nothing about such a need and neither do the other references before the Examiner. It is well

established that for two art references to be combined and used to render an invention obvious, there must be some motivation to combine them. *In re: Jones*, 958 F.2d 347 (Fed. Cir. 1992).

Claims 13 and 14 stand rejected over CenterWatch and Colon as applied to claim 1 and further in view of Clinmark. Regarding claim 13, the Examiner alleges that Clinmark discloses:

> wherein a determination is made to provide the person or caregiver with the notice in step (c) in accordance with a geographic location of an investigator associated with the study.

The specific paragraph cited by the Examiner, however, (containing the phrase "searched for oncologists in the United States") was discussing a *director of clinical affairs* searching for *oncologists* to *conduct* a clinical study, not a *person or caregiver* looking to *participate* in a *clinical study*. In fact, the second paragraph on page 2 states that "Clinmark allows pharmaceuticals, biotechnology, medical device and diagnostic companies worldwide to search profiles...." The second to last paragraph on page 2 states "In addition to its databases, Clinmark's online community provides a forum for ...individuals... to gather and learn about trends in the industry and exchange ideas." It is clear that Clinmark does not teach persons or caregivers searching the database and in fact, Clinmark teaches away from persons or caregivers searching a database. Therefore Clinmark does not teach the element "wherein a determination is made to provide the person or caregiver with the notice in step (c) in accordance with a geographic location of an investigator associated with the study."

Even if it could be shown that Clinmark did teach such an element, the Examiner has not indicated any motivation in Clinmark to combine such references. Withdrawal of this rejection is respectfully requested.

Regarding claim 14, the Examiner alleges that Clinmark discloses:

> wherein the answers submitted by the person or caregiver are provided by telephone, regular mail, facsimile, and other off-line sources.

Again, Clinmark does not teach persons or caregivers searching for clinical studies. Therefore, it can not be inferred from the use of the word "registration" and a telephone number that persons or caregivers can give registration information by telephone.

Even if it could be shown that Clinmark did teach such an element, the Examiner has not provided any proper motivation to combine such references. While the Examiner has argued that such a motivation is to provide information in a convenient manner for the requestor, that is not a motivation to use Clinmark, in particular, because Clinmark, even assuming it provides information in a convenient manner, is not the only mechanism to do so. The asserted combination is therefore improper.

Claim 15 stands rejected over CenterWatch and Colon as applied to claim 1 and further in view of Larkin. The Examiner alleges that Larkin discloses:

> wherein the step of automatically determining further includes reference to genetic sequence information associated with a person registered in the database.

Applicants respectfully disagree. Larkin says nothing about including reference to genetic sequence information. The Examiner specifically cites the section that says "the Epilepsy Foundation uses the web to recruit for its international gene discovery program." Larkin offers absolutely no information regarding the international gene discovery program and certainly does not teach including reference to genetic sequence information. Withdrawal of this rejection is respectfully requested.

Even if Larkin did teach such an element, the Examiner has not indicated any motivation in Larkin to combine such references. Stating that the motivation is learning about trials in specific diseases is insufficient. The Examiner has not shown where Clinmark, or any other reference, suggests that Larkin's teachings be combined with the teachings of CenterWatch, nor has the Examiner shown that CenterWatch suggests such a combination. Withdrawal of this rejection is respectfully requested.

Conclusion

In view of the above, the presently pending claims in the application are believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims and to pass this application to issue. The

Examiner is invited to contact either of the undersigned, at (202) 942-5721 and (202) 942-5085 respectively, with respect to any unresolved issues remaining in this application.

Respectfully submitted,

Danielle Edwards

Joseph Micallef (Reg. 39,772)
Danielle M. Edwards, Law Clerk (Reg. 51,645)

Date: March 4, 2003

ARNOLD & PORTER, LLP
555 12TH Street, N.W.
Washington, D.C. 20004
(202) 942-5000 telephone
(202) 942-5999 facsimile

Marked-Up Specification

Page 19, first paragraph under "System Architecture":

Referring first to Figure 1A, in that figure is depicted computer network 103 operatively connecting computer system 100 to [more] one or more additional computer systems represented here as computer systems 101 and 102. Computer system 100, described in more detail below, may be any of a number of commercially available computer systems, including a conventional server or workstation. Such systems may include, for example, one or more microprocessors, computer memory, conventional communication circuitry (e.g., a modem) and other commonly available peripherals. Computer systems 101 and 102, and other computers that interface with network 103, may also be such workstations or servers, or may comprise any type of commercially available personal computers capable of communicating over a computer network. Those of ordinary skill in the art will recognize that network 103 may connect to any number of additional computers. Network 103 represents a public or private computer network. The Internet is one example of such a network, though other types of networks are possible within the scope if the inventions described herein.

Marked Up Claims

2. (Amended) [The method of claim 1, further comprising the steps of:] A method for recruiting a person to participate as a subject in a clinical study, comprising the steps of:

(a) presenting one or more web pages that allow the person or a caregiver associated with the person to register with a database by submitting registration information to the database, wherein the registration information includes at least a geographic location of the person, at least one disease condition of interest to the person, contact information, and permission information indicating whether the person or caregiver wishes to receive notice of one or more clinical studies;

(b) automatically registering the person or caregiver with the database upon receipt of the registration and permission information;

(c) after step (b), automatically determining, in accordance with the permission information and the registration information, whether to provide the person or caregiver with notice of a given clinical study associated with a disease condition of interest to the person;

(d) providing the person or caregiver notice of the given clinical study only if a determination is made in step (c) to provide such notice;

(e) automatically presenting a questionnaire associated with the given clinical study to the person or caregiver after step (d); and

(f) storing answers submitted by the person or caregiver in the database.

3. (Amended) The method of claim 2, further comprising the step of:

(g) accessing the [information stored] answers to the questionnaire along with other information in the database to determine whether the person qualifies to participate as a subject in a clinical study different from the given clinical study after step (f).

4. (Amended) The method of claim [1] 2, wherein the questionnaire includes criteria [specified by a sponsor of the] specific to a clinical study for determining whether the person is an eligible subject for the given clinical study.

5. (Amended) The method of claim [1] 2, wherein steps (a) and (b) are performed during a registration visit by the person or caregiver to a web site associated with the one or more web pages, and step [(d)] (g) includes notifying the person or caregiver of the given clinical study during a current or subsequent visit of the person or caregiver to the web site.

7. (Amended) The method of claim [1] 2, wherein the notice provided in step (d) is sent by electronic mail from a web site associated with the one or more web pages to an e-mail address of the person or caregiver.

8. (Amended) The method of claim [1] 2, wherein the notice provided in step (d) is sent by regular mail to the person or caregiver.

9. (Amended) The method of claim [1] 2, wherein the notice provided in step (d) is communicated by telephone to the person or caregiver.

10. (Amended) The method of claim [1] 2, wherein a determination is made to provide the person or caregiver with the notice in step (c) in accordance with a geographic location of the given clinical study.

11. (Amended) The method of claim [1] 2, wherein in step (c) a determination is made not to provide the person or caregiver with notice of the given clinical study.

12. (Amended) The method of claim [1] 2, wherein in step (a) the registration information includes [a user id, a password, electronic mail address or telephone number, zip code, first name or preferred name, gender, date of birth,] whether the person is interested in clinical study information, whether the person is interested in new medical therapies, or whether the person is interested in participating in clinical studies.

13. (Amended) The method of claim [1] 2, wherein a determination is made to provide the person or caregiver with the notice in step (c) in accordance with a geographic location of an investigator associated with the study.

15. (Amended) The method of claim [1] 2, wherein the step of automatically determining further includes reference to genetic sequence information associated with a person registered in the database.